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#### Contribution of the COVID-19 Scientific Council

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# "ONE HEALTH" – A SINGLE HEALTH HUMAN, ANIMAL AND ENVIRONMENTAL HEALTH: THE LESSONS OF THE CRISIS

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Like the other opinions of the Scientific Council, this opinion is intended to be made public.

### **PROLOGUE**

The COVID crisis in which we have been living for two years brings a number of observations and encourages us to project ourselves into the post-crisis and the management of future crises. The Scientific Council, whose mission is to enlighten the authorities in the management of the present crisis in the light of scientific data, wishes to share in an unprecedented exercise his thoughts on a concept that he considers urgent to develop in order to introduce a multisectoral organization of health: the concept "One Health" or "A single health". This complex subject, including issues of prevention and emergency preparedness, can only be analyzed at all scales from local to international, which explains the inclusion in this document of elements on a global scale, even if an emphasis is placed on recommendations at the national level in paragraph IV.

The One Health concept goes far beyond the prevention of health crises and is closely linked to a holistic vision of health and to the links between health, quality of the environment (water, air, etc.), climate, food and agriculture and biodiversity, but this opinion remains focused on the importance of developing and operationalizing this concept in order to be better prepared for future infectious emergences. Similarly, if the behavioral dimension is essential in the prevention and management of crises, this opinion focuses on recommendations in terms of intersectoral organization, research and education to better integrate the One Health approach.

#### **SYNTHESIS**

- (i) The WHO clearly defines health as "a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity". However, health remains mainly seen through the prism of diseases affecting humans. Environmental preservation, animal health and the sustainable health of a territory remain absent from this definition. In order to have a more global vision of health, we must rethink our way of approaching the concept of single health by better integrating the environment and thus apprehending globally the health of all living organisms in a given ecosystem. We therefore wish in this text to recall the urgency of moving from a unambiguous vision of health to an integrated, more encompassing and holistic vision.
- (ii) The COVID crisis has demonstrated the need to implement integrated health approaches and in particular the "One Health" approach. This translates into a

- organization and multi-sector, multi-disciplinary, multi-actor actions at all levels, local, national, regional and global.
- (iii) In the light of the COVID-19 pandemic crisis, the One Health approach requires in particular to strengthen the interaction between science and decision-making:
  - Rethink global health governance to include One Health; Promote the
  - development of regional One Health networks, particularly in emerging areas;
  - Organize inter-ministerial collaboration in France for a global and concerted approach to better anticipate, prevent, detect as early as possible and manage crises. Measures must be taken to jointly prevent and monitor the major risks of emergence and to involve all sectors and actors from the start of health crisis management by removing administrative blockages and promoting the circulation information and data. The link between science and decision-makers is an essential component of the system, as well as reinforced coordination between the ministries of health, agriculture and ecological transition, but also research and the MAE.
- (iv) The One Health approach involves concrete research and monitoring actions on emergences, from their prevention to their management, including anticipation and early detection at the national, regional and international level. These actions can take advantage of the anchoring of scientific cooperation between France and the countries of the South by promoting "South-South" partnerships/studies.
- (v) It requires a paradigm shift in the training of health professionals and decision-makers, the development of an education in complexity that would allow the acquisition of skills that can be mobilized in many other contexts (biodiversity, climate change, ecological transition ...). The approach One Health could thus become an ambassador for many other issues with a determining societal impact in the medium and long term.

The pandemic crisis therefore commits us to collectively implement institutional changes, transdisciplinary research activities, concrete actions in the field based on the social fabric, redesigned training and education for all - including our decision-makers. - in order to be better prepared for future infectious emergences through a One Health approach.

### INTRODUCTION

Like about 75% of emerging diseases listed in humans, COVID-19 is most likely a zoonosis due to the introduction of a coronavirus from an animal reservoir. Known for a long time in animal health as in human health, coronaviruses are a family of viruses (seasonal coronaviruses such as OC43 or NL69, avian infectious bronchitis coronavirus, etc.), some of which have demonstrated their risk of dissemination to humans. (Mers-CoV in 2011, SARS in 2003).

The current crisis highlights the need to be able to identify risks upstream, to prevent and limit them, and to anticipate emergences in order to better prepare for future health crises, including pandemic crises. This objective of anticipation and warning requires the identification of all the partners (researchers, decision-makers and actors in the field involved in monitoring and warning), the definition of objectives, then the implementation of organizational milestones, and decision-makers.

This approach can only materialize in an integrated and intersectoral manner (human health and animal health, but also the environment) through a strategy: One Health or One Health. (we will only use this term to define integrated health approaches at the interface between human health, animal health and the environment, cf. framed the definitions of the different integrated health approaches). The example of the pandemic crisis shows that the study and understanding of emergencies in general require a detailed analysis of the interdependence of these sectors, with a transdisciplinary vision, which requires both the production of knowledge upstream allowing to understand the mechanisms of transmission and adaptation of a zoonotic pathogen to humans, and to develop or improve monitoring and early detection tools downstream.

The consideration by public policies of issues related to the interactions between health and biodiversity is recent. The mobilization of several organizations in the health and biodiversity sectors has only been established at the international level since the mid-2000s. The WHO, the FAO and the OIE declared in 2010 that it would be appropriate to achieve "a world capable of preventing, detecting, containing, eliminating and responding to risks to animal and human health attributable to zoonoses and animal diseases that have an impact on food safety".

The same approach was developed at the Rio+20 conference in June 2012. A joint report drawn up by the World Health Organization (WHO) and the secretariat of the Convention for Biological Diversity (CBD), beyond d affirmation of the links between health and biodiversity, underlines the need for more integrated policies.

These initiatives are part of the "One Health/One Health" concept which aims for an integrated approach to all aspects of human health, animal health and ecosystem management. This concept clearly highlights the need for policies integrating human health and biodiversity.

In light of certain flaws in the management of the COVID crisis, it is clear that this One Health strategy, which is beginning to impose itself in the continuity of reflections around global health, is culturally little shared, currently poorly structured, not sufficiently operational and difficult to read. Its implementation, necessarily progressive, requires a precise timetable describing the steps to be taken, with the focus of reflection on the decision-making processes: what global/world health should represent and what place should be given to it both at the scientific level as politics at all scales.

Beyond crisis management, it is the structuring of a consolidated, responsive and integrated multi-sector organization at the highest level of health governance that needs to be proposed.

### Definitions of the various integrated health approaches

**The "One Health" concept**aims to highlight the relationships between human health, animal health and ecosystems and to make the link between ecology and human and veterinary medicine. The "One Health" approach focuses primarily on infectious diseases, whether transmitted from animals to humans or vice versa, their emergence in connection with global changes, antimicrobial resistance, and food safety.

**The "EcoHealth" concept**advocates an ecosystem approach to health, tending to focus on environmental and socio-economic issues. It was originally designed by disease ecologists who work in biodiversity conservation.

**The concept of "planetary health"** takes into account the planetary physical and biological limits within which health, well-being and equity for humanity can develop, politically, economically and socially. In other words, planetary health considers the health of human civilization and the state of the natural systems on which it depends.

**Overall health**emphasizes the convergence of health issues (e.g. emerging viruses, antibiotic resistance, chronic diseases) and health determinants (e.g. nutrition, smoking, environmental pollution) on a global scale, and on the interdependence between countries of public health responses to these issues.

**environmental health**includes aspects of human health, including quality of life, that are determined by the physical, chemical, biological, social, psychosocial, and aesthetic factors of our environment

### I. WHAT WAS MISSING DURING CRISIS MANAGEMENT?

The deployment of a One Health strategy should in particular make it possible to analyze and characterize the zoonotic risk in order to limit it. Its upstream use aims to prevent emergence and re-emergence through prevention and control actions such as: monitoring in reservoirs, particularly bats, understanding and implementation of measures for emergence factors to limit their impact.

### HAS.THE CONCEPT OF CROSSING THE SPECIES BARRIER

Risk control requires understanding the different stages of crossing the species barrier, ranging from transfer to adaptation of the new pathogen to its new host, humans, which makes it possible to know the mechanisms leading to the appearance of a causative pathogen *ultimately* of a pandemic. For the COVID crisis, even if the emergence process implemented is not fully known, virological surveillance by RT-PCR and serology of bats, wild and farmed animals, and humans in contact with animals could have detected this new coronavirus before or as soon as it emerged in humans and preempt its epidemic spread. This monitoring is broken down into several stages including:

- Detection of coronavirus in bats; Analysis of the level of
- circulation of this virus in this reservoir;
- Identification of potential intermediate hosts for wildlife and farm animals;
- The mechanisms of transmission then of adaptation of the viruses to these different hosts (intermediate reservoir);
- The analysis of the diffusion capacity of the coronavirus in this new host, the level of circulation in the monitored populations, the situations that can lead to the spread of the virus from these different reservoirs to humans, for example the live animal markets including from wildlife, and its adaptation to humans.

This understanding of the mechanisms of transmission to humans also presupposes being able to detect early the first rare cases in humans and to take them into account.

### **Principle of species barrier research**

A number of pathogens, especially viral ones, are zoonotic infectious agents. This means that they are hosted in animals, sometimes without being associated with infectious manifestations, and that they can occasionally be responsible for a

human infection. These infections can be either rare sporadic or infectious dead ends, and do not cause secondary cases in humans, or conversely be the cause of a wider spread or by a fortuitous evolution in the initial host, either by secondary adaptation in humans or an intermediate host. Thus, avian Influenza viruses, whose reservoir is aquatic birds, can adapt to humans by a mechanism of genetic reassortment and/or mutations occurring during infections in pigs, which are the intermediate host. These viruses can then be perfectly adapted to humans and be responsible for chains of transmission and therefore pandemic risk. The pathogen can also undergo a fortuitous adaptation/mutation in its host, such as for example the Chikungunya and Zika viruses,

Each time, the zoonotic virus must undergo an evolution which allows it to be adapted to humans, or to an intermediate host. These unpredictable evolutions are favored by the high level of circulation of the pathogen in its reservoir, and by the proximity between the reservoir, humans and the intermediate host and/or the vector. These changes are sometimes predictable, sometimes unexpected. Close monitoring of the pathogen in its reservoir makes it possible to monitor the risk, and to anticipate a possible introduction into humans.

Crossing the species barrier sometimes leads to serious infections, when the virus is in equilibrium in its natural host, but it causes fatal or serious infections in humans (e.g. rabies, Herpes B of the monkey, nipah). Under these conditions, the infection is due to direct exposure of humans to the infected animal through a bite. Again, this zoonotic pathogen causes an infection in the infected person, without there being a chain of transmission.

Understanding the mechanisms of transmission and adaptation of these zoonotic viruses to humans is the basis of research on crossing the species barrier.

### **B.RETRO-ZOONOSIS**

Once the virus has adapted to humans, the question of a return to animals and its consequences can arise.. SARS-CoV-2 evolved from an animal reservoir to adapt to humans. This recent zoonotic origin explains why the possibility of a "reverse" infection in a reservoir other than humans is possible, more particularly in mustelid mammals. This retro-zoonotic component has already been observed with the infection of mink farms in Europe, in particular in Denmark, followed by a reintroduction of the virus in humans. Today, the SARS-CoV-2 virus has been detected in 32 countries in 17 animal species, including mink but also cats, dogs, lions, tigers and more recently deer in North America, where it seems to have spread very broadly.

During episodes of retro-zoonosis, the virus carries out a certain number of adaptation mutations to its new animal host, leading to modifications in the internal genes and in the spike protein. These mutations lead to a modification that can be very significant for viruses, with a significant risk of acquiring severity factors and/or immune escape. For example, a recent article suggests (without proving it) that the Omicron virus could have been a virus which emerged due to a retro-zoonosis.

This theoretical evolution of the virus makes it necessary to monitor the circulation of these viruses in different potential reservoirs, where the virus has already been introduced, and to conduct strict control measures to avoid any retro-zoonotic episode, such as of what is being done to prevent avian flu.

It should be noted that the risk of retro-zoonosis not only adds adaptation mutations, but also a risk of genetic recombination with another zoonotic virus, the circulation of beta-coronaviruses in different reservoirs being very frequent.

Knowledge of all these transmission stages aims to limit the passage from one to the other, but also to transmit information on the level of risk at a given moment to all the surveillance actors, but also to decision-makers. Knowledge of the level of risk also allows the rapid implementation of diagnosis, screening, diagnosis, and sequencing for monitoring and risk analysis purposes (identification of molecular markers of adaptation when crossing barriers of 'species).

### **vs.INSUFFICIENT JOINT ACTION BY THE DIFFERENT ACTORS**

This strategy is only possible if the players in human health, animal health and the environment are able to unite their thoughts and act together. This joint action requires not only close communication around risk analysis, but also collaboration during crisis management. In the case of the COVID crisis, apart from viral surveillance in domestic and wild animals alone in order to establish recommendations based on risk analysis, earlier and greater involvement of the world of animal health and better articulation with the world of human health would certainly have had added value by:

- His knowledge of coronaviruses in animals (species concerned, capacity for evolution, control of epizootics, development of vaccines, deployment of vaccination, resistance to different types of countermeasures);
- Its capacity for diagnostic tests and screening in the veterinary laboratory, and mass sequencing;
- Its proven experience in managing health crises at the population level: largescale diagnosis, active and passive surveillance, seroprevalence, research

and characterization of pathogens, vaccination, etc. See as an illustration in the box the experience of controlling avian infectious bronchitis by vaccination, which can make it possible to learn lessons about SARS-COV2 or at least allow hypotheses to be posed on the advantage of heterologous vaccination.

This collaboration, particularly in the field of screening and diagnosis, is not self-evident. There are many pitfalls to its implementation, both cultural and logistical as well as organizational, administrative and regulatory. The establishment of close collaboration and coordinated response plans must make it possible to resolve these difficulties and must be prepared. It is also essential to coordinate at the highest level of health governance the organization of this operational field response both for the individual response (management and care of cases) and for the collective response (management of the epidemic ).

### <u>Data on vaccination in birds against bronchitis coronavirus</u> <u>avian infection (N. Eterradossi, G. Salvat, B. Grasland, P. Brown; ANSES)</u>

Avian infectious bronchitis is a disease of poultry of the genus Gallus associated with infection of the latter by a Gammacoronavirus (IBV). The disease, first described in 1931, is very highly prevalent in chickens. Its vaccination prevention has been in place since the 1950s and today is almost systematic in breeding.

The use of live attenuated vaccines (often administered by nebulization to induce optimal local immunity by stimulating the respiratory and ocular mucous membranes in young subjects) during the first 8 weeks of age is supplemented by booster vaccinations carried out in subjects intended for longer rearing using adjuvanted inactivated vaccines, administered subcutaneously or intramuscularly.

The emergence of new serotypes of the IBV virus is a challenge for poultry veterinarians and has led the veterinary pharmaceutical industry to try to adapt vaccine strategies against infectious bronchitis in order to induce as broad a vaccine protection as possible, capable of controlling different serotypes of IBV. The inclusion, within the same vaccine program, of a combination of vaccine antigens representative of different serotypes is today a very commonly used approach: live attenuated vaccines derived from different IBV serotypes (Mass, 4 /91, also called CR88 or 793B, QX), as well as multivalent inactivated vaccines combining several of these serotypes, now have marketing authorization.

Primary vaccination with a historic strain followed by a booster with an antigenically different variant strain confers greatly increased protection both in terms of antibody levels and coverage spectrum against the variants (capacity to neutralize viral serotypes yet not included in the vaccine programme).

In the presence of pre-existing heterologous vaccine immunity, significantly less viral diversity is observed in the propagated IBV population.

These data are certainly not entirely extrapolable to the vaccine programs used against human infection by SARS-CoV-2. Significant differences exist between the immune system of birds and that of mammals. The vaccines used in birds are either live attenuated or inactivated and are therefore not in all respects comparable to the vaccine valencies currently used in humans, whether they are mRNA or protein. Nevertheless, the results obtained with a long historical perspective on the vaccination of birds raise questions about a possible possibility of increasing the vaccine protection of humans against variants that escape vaccination by the booster use of an antigenic valence. different from the initial strain currently used.

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### II. WHAT IS UNDERWAY TO STRENGTHEN ONE HEALTH APPROACHES?

### **HAS.IN RESEARCH**

More than a concept, One Health is a strategy deployed for a long time in research and surveillance with numerous projects on zoonoses in areas of emergence and reemergence of Ebola, Mers-CoV, avian influenza, Nipah virus, vector-borne diseases, rabies, etc. or regionally by setting up surveillance networks, such as One Health Indian Ocean or Sega One Health.

### Example of a One Health approach to anticipate the emergence of the Nipah virus in Southeast Asia

Nipah virus (NiV) infection is an emerging and serious zoonosis in animals and humans. This virus has a high fatality rate in humans, with more than half of infected people dying from it. Since its appearance in 1998 in Malaysia and Bangladesh, it has caused the death of more than 500 people. Human-to-human transmissions have been observed, which makes this virus a particularly monitored pathogen.

CIRAD and the Institut Pasteur are carrying out multidisciplinary research aimed at better assessing the risk of NiV emerging in Cambodia and its transfer to domestic animals or humans. Researchers in ecology, epidemiology, modelling, virology, genetics, but also in anthropology associate their work with conservators and local authorities in order to take into account the conservation aspects of the species, in this case the bat which is the host of infection.

In order to detect the presence of the virus, virological tests were carried out on 3000 bats and on 420 people in contact with these animals. Mobility (tracked by GPS), population dynamics, diet and the presence of NiV in urine were studied in a colony of "Lyle's flying foxes" (Pteropus lylei). At the same time, the agricultural and food practices of local communities were monitored.

These studies have shown the existence of seasonal patterns in both animal population dynamics and virus circulation. They have made it possible to identify certain periods when human practices can expose them to a higher risk of infection or even areas where contact between humans and bats is more numerous. The interviews also showed limited conflicts between humans and bats, as well as the absence of risk perceived by the local communities. In order to educate populations on the risks associated with their practices and the characteristics of flying foxes, an integrative model is being developed which should allow the use of preventive measures reconciling public health and the conservation of animal species.

#### References:

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### <u>Issues related to emergence and re-emergence in 2022</u> filovirus infections (Ebola, Marburg)

The rapid sequencing of the viral genome carried out by next-generation sequencing methods during filovirus epidemics produces important epidemiological information. It documents a reliable and up-to-date picture of the chains of transmission and the evolution of viral sequences, thus contributing to the appropriate response to the epidemic event. These procedures make it possible to qualify the mode of contamination of the index cases of epidemics, differentiating epizootic transmission (from wild fauna, large primates, antelopes) from the resurgence of the viral strain responsible from a human reservoir formed during a previous epidemic. This fact is important given the existence of a human reservoir with persistence of the pathogen formed during the two recent major Ebola epidemics in West Africa (2014 and 2016) and in the eastern region of the Democratic Republic. of the Congo (in 2018). This recourse allows decision-making assistance in public health integrating an important ethical dimension, insofar as the people constituting these unprecedented reservoirs are exposed to a risk of social stigmatization and to a triple constraint comprising:

- Survivor Syndrome;
- Chronic Illness Syndrome or Prolonged Symptoms;
- Post-trauma syndrome linked to being at risk of transmission, and an increased risk of stigmatization and isolation.

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### Rift Valley fever in Mayotte: an example of One Health monitoring and modeling

Rift Valley fever (RVF) is a zoonotic viral disease found mainly in parts of Africa, Mayotte and the Arabian Peninsula. It mainly affects cattle, causing waves of abortion and high mortality in the youngest animals. Humans can become infected through direct contact with the bodily fluids of infected animals or through the bites of infected mosquitoes from sick animals. While most patients develop asymptomatic or mild forms, the disease can in rare cases (1 to 3% of patients) progress to severe forms, characterized by ocular and meningeal disorders as well as hemorrhagic fever which can lead to death. .

Since 2008, the implementation of two surveillance systems in Mayotte, one centered on animals, the other on humans, has made it possible to collect a great deal of quality surveillance data on RVF. These concern seroprevalence in livestock and human epidemiology (number of cases, sociodemographic characteristics, criteria for exposure to the disease, geolocation, etc.).

Inserm, Public Health France and CIRAD have developed a mathematical model integrating all these data in order to reproduce the dynamics of virus transmission during the 2018-2019 epidemic. This model shows that transmission of the virus to humans via mosquitoes was greater than transmission via direct contact with infected livestock. Modeling the potential impact of vaccinating livestock to reduce the scale of the outbreak shows that vaccinating 20% of livestock could reduce the number of human cases by 30%. Early and massive cattle vaccination campaigns are therefore an essential measure to reduce the incidence of the disease in humans.

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### **B.GEOPOLITICAL VISION**

Beyond these research approaches, there has been real political awareness recently and in the world with emblematic actions: this is also the case in France, but with less visibility.

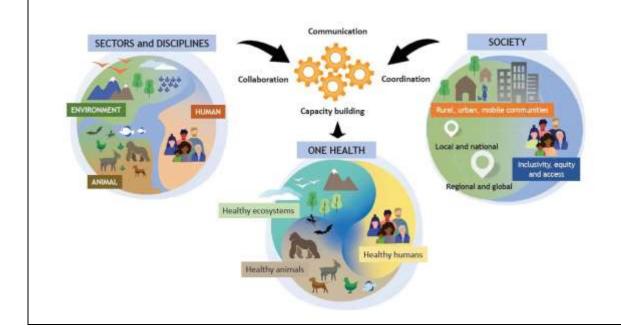
### **Internationally:**

 A Franco-German presidential statement in October 2020 at the Peace Forum politically launched the idea of One Health expert advice. This idea was then taken up by the tripartite bringing together the WHO, the OIE, and the FAO joined by UNEP, an initiative leading to the definition of the terms of reference of a "One Health High Level Expert Panel" (OHHLEP). This committee, officially set up on May 20, 2021, is made up of 26 independent experts from various geographical origins and multiple disciplinary skills. These experts will be responsible for gathering, analyzing, disseminating and giving greater visibility to the scientific information available on the links between human, animal and environmental health. With the objective of helping political leaders and international organizations to take useful decisions to prevent and respond to future health crises,

One of the first tasks of OHHLEP was to propose ainclusive definition of One **Health**. This was published in a joint WHO, OIE, FAO UNEP statement on 1<sub>er</sub> December 2021:

The principle**"One Health »**consists of an integrated and unifying approach that aims to balance and sustainably optimize the health of people, animals and ecosystems. It recognizes that the health of humans, domestic and wild animals, plants and the environment in general (including ecosystems) is closely linked and interdependent.

The approach mobilizes multiple sectors, disciplines and communities at different levels of society to work together to foster well-being and address threats to health and ecosystems. It is also about meeting the collective need for clean water, clean energy, clean air, and safe and nutritious food, taking action against climate change and contributing to sustainable development.



- The declaration of June 4, 2021 by the G7 health ministers and that of September 5-6, 2021 by the G20 health ministers clearly promote One Health approaches and recommend in particular the strengthening of integrated surveillance actions and analyzes data in human health, animal health, food and the environment, including for the prevention of emergences.

#### In France:

- The joint opinion of the Academy of Sciences, the Academy of Medicine, the Veterinary Academy and the Academy of Pharmacy of June 8, 2021 is in favor of a decompartmentalization between management of human health and animal health, particularly in terms of scientific training and the acquisition of transversal skills for future health professionals and decision-makers.
- On June 17, 2021, the Veterinary Academy adopted a new definition of veterinary public health: it is all collective actions, mainly sovereign, in relation to wild or domestic animals, their services and their productions entering in particular into the food chain, which aim to preserve human and animal health including the state of well-being and the health of ecosystems. It thus contributes to sustainable development and the implementation of the "One Health" concept.
- The parliamentary report chaired by MP Elisabeth Toutut-Picard (December 2020) recommending, among other things, that prevention research be associated with curative research in environmental health.
- The creation of the ANRS-MIE agency and the acceleration strategy implemented by the Ministry of Research on Emerging Infectious Diseases, which take into account and integrate the One Health approach into their strategy.
- The integration of a veterinarian into the COVID-19 Scientific Council in February 2021 is emblematic of the approach to decompartmentalising human health animal health in crisis management.

### III. WHAT NEEDS TO CHANGE OR ACCELERATE?

It is essential to prepare a roadmap for the implementation of a real One Health approach in France to optimize the French positioning at the international level, and internationally. This roadmap must have strong leadership and institutional support and be envisaged with an interministerial decision-making level and regional application. It seems necessary to build this approach on the basis of what already exists.

### A multi-step process:

## HAS. TAKE NOTE OF A WIDE SCOPE OF ACTIONS AND INVESTIGATIONS FROM PREVENTION TO INSTITUTIONAL MANAGEMENT OF A HEALTH CRISIS

This holistic approach presupposes the development of multiple levers covering the four pillars of what a global health approach should be, i.e.:

- · Prevention and health education;
- · Crisis preparation;
- Early detection;
- Intervention for purposes of control and mastery.

These various complementary pillars presuppose a certain number of prerequisites of knowledge, based in particular on the understanding of the links biodiversity-agriculture-food-health, on the notion of sharing transdisciplinary information and the development of indicators.

This global knowledge will make it possible to co-construct economically viable socio-ecosystems (ecosystems integrating humans and their social system) upstream of the appearance of the risk, with characteristics unfavorable to emergences and offering more resilience to health crises.

**The development of indicators**based on innovative tools, capable of combining surveillance and alert, is essential to facilitate intersectoral and multidisciplinary collaboration which will make it possible to identify risks, define alert thresholds and corrective interventions in the short, medium and long term.

These adapted responses presuppose a rapid decision-making process, with institutional support adjusted both to ensure the acceptability of rapid responses by the various socioeconomic actors and political decision-makers. As such, it would be appropriate to reflect and propose an operational model on "alert-decision" interactions, the latter being based on a necessary robust and recognized scientific basis.

### B.MOBILIZING THE RESEARCH SECTOR ON THE ONE HEALTH APPROACH, IN FRANCE AND ABROAD

It seems important that the actors of research in France are mobilized on the understanding of the risks and their analysis. This stage, which requires combining fundamental, translational, but also pragmatic research (operational field research), will lead to the construction and testing of prevention, detection and alert tools, in a logic of anticipation.

Upstream research is essential to irrigate the fields of translational and operational research by integrating all aspects of animal health, the environment and human health. This research should in particular focus on innovative approaches in metagenomics (unprejudiced detection of circulating pathogens in reservoirs and animal vectors, molecular identification of viruses with zoonotic potential, etc.), modelling, artificial intelligence and socioeconomic studies. This research is thus based on multidisciplinary, multisectoral and multiprofessional projects, in an approach necessarily covering all geographical scales and therefore essentially international.

Several recent One Health-type research initiatives on emergences could be consolidated quickly, in particular:

- The Prezode International Initiative "Preventing Zoonotic Disease Emergence" launched at the One Planet Summit on January 11, 2021 by the President of the French Republic aims to strengthen One Health surveillance networks around the world as well as to develop integrated prevention strategies to reduce the exposure of human populations to zoonoses. Initial French funding of 60 million euros has already made it possible to bring together all the different actors in research, animal health, human health, the environment, decision-makers and surveillance actors. This initiative has received the support of 7 governments and more than 100 organizations in 40 countries.
- The ANRS-MIE Agency and its PEPR funding program (Priority Research Programs and Equipment): The priority objectives of this program will be to better understand emerging infectious diseases, prevent them, and control them in an effective and integrated manner at both individual and global levels by working on the continuum of animal health, environment and human health. This program is based on interdisciplinary and multi-institutional research combining research in the human and social sciences and participatory research. This research program is original because, in addition to its global approach, it is organized according to two temporalities: (i) reaction in the acute crisis phase (emergence or re-emergence, epidemic or even pandemic); (ii) research work in "inter-epidemics", in the longer term, to

prepare the response to future epidemics and analyze the determinants of emergence and their spread.

• National Environmental Health Plan (PNSE4): This Plan is based on inter-ministerial collaboration between four ministries (ministries responsible for health, ecological transition, foreign affairs, agriculture and food, MESRI). It has just been adopted and includes 20 operational actions. The principle of creating a transversal "One Health" group, guaranteeing the consideration of this concept, has been recorded. He will be in charge of managing certain actions in the field of training, research and wildlife health and he will check the proper integration of the concept in the other actions. It will participate in the definition of indicators and will ensure interactions with other plans such as the National Biodiversity Strategy and the Ecoantibio 2 plan.

A response and an organization centered solely on France would be unsuitable for monitoring risks imported from other regions of the world.. Coordination between the various One Health international initiatives should make it possible to pool efforts and create synergy in research and surveillance

### vs.<u>INITIATE A TRANSFORMATION OF PROFESSIONALS AND CIVIL</u> SOCIETY

Contribute to the implementation of the concept "**one health**" will require time to produce operational effects. Already, be part of a training process in order to abolish the borders between the health sectors:

It is necessary to change the paradigm to achieve a transformation of the approaches still too centered on the medical profession and on the disease. Recognizing that "man is a constitutive, but not unique, part of planetary ecology and that he maintains a link of interdependence with the rest of life" (Philippe Descola) would naturally abolish the boundaries between health sectors .

### -A necessary innovative transdisciplinary training for professionals and the public

The first step is to lay down the principles allowing each field of disciplines concerned to define the possible contributions of each: Who can intervene, with what contributions and what objectives in a global approach?

For the medical professions in the broad sense, veterinarians, pharmacists, biologists and ecologists, it is suggested to complement the initial training with continuous professional development. A cross-disciplinary training reference should be built together.

This widely open training will be based on cross-disciplinary teaching modules involving multidisciplinary expertise, combining public health, population health, territories and environment, research and development. It will have to be "integrated" into the ongoing reform of public health training, including for non-health professionals. The fact of teaching One Health concepts early in the curricula of each discipline will later facilitate the collaboration of professionals in a "natural process" and obvious sharing.

Beyond this audience of professionals, raising awareness and even training in One Health for decision-makers, teachers and educators from civil society will be able to produce an education and a culture shared by the entire population. This education should be conceived in the school career from college.

In addition to these specific training courses, cross-disciplinary skills should be developed to understand the One Health concept: critical thinking, complex thinking, systemic thinking, the ability to multidisciplinarity, the ability to collaborate and the culture of 'uncertainty. An important challenge will also be to bring together the actors of civil society, in particular associations, who often evolve in different bubbles without always knowing each other.

### **D.INITIATE INSTITUTIONAL CHANGES AT ALL SCALES**

### Worldwide:

The management of diseases inherent to globalization cannot be mastered on the scale of a single country i. Several institutions and structures should evolve to face the global challenges posed by global health:

- It is essential that the WHO and the global health governance undertake a profound reform in order to integrate a true One Health approach.
- The WTO and free trade agreements must integrate the health, environmental and social elements inherent in production and transport that can result in binding and regulatory actions on livestock, wildlife trade, food imports ....
- The recommendations of the new OHHLEP expert panel (One Health High Level Expert Panel) should be implemented through regional or national operational activities with the support of international organizations).
- The implementation of One Health approaches with the least advanced countries in the field of health management will have to be supported through twinning programs, for example European, as during the Ebola crisis in West Africa in 2014 -2016.

**At the regional level between countries**"in the South and in the North", sharing the same risks or the same socio-economic and political constraints:

- One Health approaches must be integrated into European health and complete the strategy presented by the Commission on November 11, 2020 ("Building a European Health Union: a Europe better prepared for crises and stronger in its response"). Such a construction requires that the privileged relations between countries within the European space be taken into account and to include in the discussions the countries located at the border of the European space.
- Existing One Health regional health and surveillance networks should be developed with sharing of human resources between sectors and between willing countries.

France can greatly contribute to this regional vision through its partnership networks and its establishments in overseas regions and its activities in partnership with the South (health and research networks, Cirad Partnership Devices, IRD International Joint Laboratories, network of Instituts Pasteur, Inserm laboratories and ANRS sites, etc. The deployment of One Health research and monitoring systems could be proposed by France at European level in emerging zones.

### At the territorial level, in particular overseas, but not only:

- A number of monitoring levers and systems could be implemented locally, in
  conjunction with national and supranational structures. These sites for
  environmental monitoring (sentinel sites) and operational monitoring of prevention
  actions (living laboratories or living labs) will make it possible to meet specific
  specifications such as the construction of socio-ecosystems that are not favorable to
  emergence and resilient to health crises. . This work should be done with research
  teams in environment and ecology in conjunction with professionals and institutions
  responsible for the health of a territory.
- This structuring should be based on a fluid and organized interface between local authorities and research teams.
- Set up experiments in collaboration between the ARS, the regional directorate for food, agriculture and forestry (DRAAF) and the regional directorate for the environment, planning and housing (DREAL) and communities to initiate pilot actions confronted with the eyes of society and promote a change of culture.

### IV. 10 ACTIONS/PROPOSALS TO STRENGTHEN THE ONE HEALTH APPROACH IN FRANCE

At the national level, many actions both at the level of research and at the level of institutions are necessary to respond to the challenges associated with health crises:

- 1. Set up a One Health interministerial platform or interministerial governance placed at the highest level of government that would combine different scientific expertise. The role of this platform would be to analyze and regularly update the major risks of the emergence of pathogens in the environment, in animals or in humans and to share them in complete transparency with all stakeholders
- 2. Establish joint animal and human health surveillance for zoonoses. This would involve strengthening the involvement of the Ministry in charge of health and Public Health France in the multi-stakeholder epidemio-surveillance platforms set up by the Ministry of Agriculture and Food. Joint monitoring of emerging viruses in the animal and human population could make it possible to anticipate an emergence in humans, provided that at least a list of pathogens to be monitored is established and that research is carried out quickly in humans. humans and animals in case of detection. As such, work has already begun with the establishment of a working group, under the aegis of the ANRS MIE, multidisciplinary of the animal world,
- 3. Strengthen the development of One Health actions between the ministries in charge of Health, Agriculture and the Environment, their agencies (in particular Public Health France and ANSES) and regional authorities (ARS, DDPP, ...) by promoting operational interactions with the animal health and environment sectors, to include One Health in a renewed vision of public health.
- 4. Promote the bringing together of the reference laboratories of the Ministry of Health (CNR) and Agriculture and Food (LNR) through joint funding, or even dual supervision
- 5. Identify emerging surveillance deficits at the human health animal health interface and redefine ministerial responsibilities: pathogens or diseases of public health interest can circulate in farms or in arthropod vectors without directly falling under the responsibility of the Ministry of Agriculture because not categorized (example of the swine influenza virus, surveillance

- H5N8 avian influenza in humans, CCHF virus in animals, etc.). The responsibility for surveillance and management of these diseases must be redefined.
- 6. Quickly implement the means of mobilizing animal health experts and human health experts from the start of health crises.
- 7. Involve the hospital, from infectiologists to resuscitators, so that they can report abnormal and severe clinical events without identified etiology (disease X), in particular if it proves to be imported. Mobilize hospital research teams on rapid and innovative diagnoses of severe infectious diseases of undetermined origin. Facilitate the rapid feedback of information as well as feedback on the follow-up of cases to advance in the diagnostic process.
- 8. Remove administrative blockages for the mobilization of research laboratories and veterinary laboratories on diagnosis and sequencing in times of crisis: facilitate for these laboratories the preparation of samples by the University Hospitals, their inactivation, their supply, also facilitate the recording of the results and their dissemination to the various actors, particularly in overseas territories where capacities are limited.
- 9. Promote research at the environment/animal health/human health interface concerning zoonoses by strengthening collaboration between institutions (ANSES/CIRAD/INRAE/INSERM/IRD/IP, etc.) and the exchange of data and information, in particular through the ANRS MIE, an agency set up to coordinate research around emerging infectious diseases. This vision incorporates the need for North-South collaboration.
- 10. Rely on French research partnership networks and establishments in overseas regions and in "southern countries" so that France is a driving force for Europe in One Health integrated research/surveillance in emerging zones by promoting "South-South" partnerships/studies.

This strengthening in France of One Health approaches in institutions, the monitoring of emergences, research and education should allow France to be more visible, even a driving force in the actions to be developed at European and international level.

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